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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,215	06/15/2001	Peter A. Crooks	50229-267	5136

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EXAMINER
KIM, VICKIE Y

ART UNIT	PAPER NUMBER
1614	11

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,215	CROOKS ET AL.	
	Examiner	Art Unit	
	Vickie Kim	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election acknowledged

Applicants affirmation on the election with traverse of Group II, claims 5-20 is acknowledged. Applicant's traverse the restriction requirement on the grounds that there would be no burden in searching the entire application. This argument is not persuasive, as not all groups encompassed by the application would be classified together. As mentioned in previous office action, each invention is found to be patentably distinct subject matter proven in numerous patent literatures. For instance, it is well known in the art that agmatine is effective cancer agent as evidenced by Merck Index(1996). US 6150419 teaches a composition of agmatine as a treatment for neuropathic pain. Furthermore, even if there were unity of classification, the search of the entire application in patent and non-patent literature (a significant part of the thorough examination) would be burdensome due to the reasons mentioned in previous office action(e.g. patentably distinct subject matter proven in numerous patent literature). Therefore, the restriction requirement is deemed to be proper and made FINAL.

Status of Application

The claims 1-20 are pending, and the elected claims 5-20 are presented for the examination. The non-elected claims 1-5 is withdrawn from consideration.

Information Disclosure Statement

Applicant's information disclosure statement received 12/27/2001(paper no. 6) has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Objections

1. Claim 8 is objected to because of the following informalities:In claim 8, line 10, the expression of Markush is not properly formulated. It seems that a typographical error is made inadvertently where the term "or" is missing right "thio, ". Appropriate correction is required.

2. In claim 13, in line 1, it seems that a typographical error is made inadvertently where the coma(,) is missing between "epilepsy" and "seizure". Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim 10 drawn to the method of treating the occurrence of epilepsy...thereof and preventing or reducing the disorder. However, it is confusing what the scope of the claimed subject matter applicant is claiming. Firstly, the phrase " a method of treating the occurrence" is not clear whether the treatment is referring to the reduction of the number of the occurrence or the severity of the occurrence. Deletion of the phrase "the occurrence" would obviate this rejection. Secondly, it is not clear how the phrase recited in line 4(i.e. " ....thereof and preventing or reducing the disorder.") should be interpreted. If Makush expression is applied to describe the claimed subject matter, the

term "and" should be replaced with the coma(,) so that the claims is written with proper Markush expression. For instance, the claim 10 should be read: A method of treating epilepsy....thereof, preventing or reducing the disorder. Clarification is required.

5. Claim 9 recites the limitation "the condition" in line 3. There is insufficient antecedent basis for this limitation in the claim.

6. The claim 9 recites "symptoms associated with the disorder" and the claim 16 recites "symptoms or features associated with the disorder". However, it is not clear what the claimed term "features" or "symptoms" is referred by, which renders the claims indefinite. The disorder should be referring to "electroconvulsive disorders" where the feature or symptom is not defined by the claim or the specification, it fails to provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

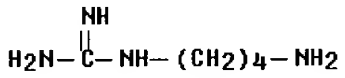
8. Claims 5-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Uzbay(Effects of agmatine.., 2000, Jan).

Claims are drawn to a method of treating, ameliorating or preventing epilepsy, seizure or electroconvulsive disorders using an effective amount of agmatine or an

agmatine analog wherein said method is achieved when said administration effectively reduces the seizure.

Uzbay teaches effects of agmatine, which is an endogenous polyamine metabolite of L-arginine, have been effectively reduced both incidence and intensity of the audiogenic seizures, see abstract, page 156, 3rd paragraph . Uzbay also teaches the underlying mechanism where the inhibitory effect of agmatine is via inhibition of Nitric oxide synthase(NOS) in the glutamate system, see page 157, left column.

As to claims 5-6, 10-12, Uzbay teaches Agmantine as an active drug that has the following structure:

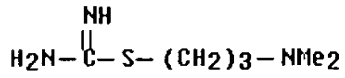


Thus, the claims are met by the cited reference's teaching.

As to the claims 7-9, Uzbay teaches drug used in the study wherein agmatine sulfate(40, 80 and 160mg/kg) dissolved in saline is injected into the subject.

9. Claims 5-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Seeley et al(abstract only, 1999).

Seeley et al teach dimaprit and its anticonvulsive activity effectively treating epilepsy by reducing the severity of seizure incidence. For instance, dimaprit (0.2-3mg/kg) has the following structure:



As to claim 6, dimaprit is encompass by the claimed structured formula when R1, R2, R3, R4, R5, n, X and Y is substituted with Me, Me, H, H, H, 2, CH2 and S, respectively. Thus, all the critical elements are taught by the cited reference.

10. Claims 5-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Cherksey et al(US 5,432,202).

US'202 teaches a spermidine-like effect on NMDA receptors by exposing a cell membrane to selected polyamines(e.g. agmantine) as effective calcium channel modulators wherein the calcium channel modulators of the patented invention also exhibits anticonvulsant activity(e.g. anti-epileptic), see column 3, lines 20-25 and column 8, lines 32 thru column 13, lines 40. It also teaches numerous compounds sharing very same pharmacorephore(HN-C(NH_2)-NH-) that is responsible for the therapeutic effects(see columns 8-14) and that results in calcium channel blocking activity. US'202 also teaches the pharmaceutical product comprising an active agent(e.g. agmantine) and a carrier, which can be formulated in oral, topical, or parenteral dosage forms with the effective dosage amount for human subject that is about 0.05-50mg/kg, see column 15, lines13.

11. Claims 5-7, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Chabrier de Lassauniere et al(WO9809653).

WO'653 teaches a NO syntase inhibitor such as agmatine(page 1, 4th paragraph) and the composition thereof, and its use in the treatment of epilepsy(page 8, 1st paragraph), see abstract. WO'653 also teaches pharmaceutical products containing NO syntase inhibitor and the excipient, see column 3, lines 13-18.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cherksey(US 5,432,202) in view of Lerman(US 64441156).

The teaching of US'202 is mentioned immediately above in 102 rejection(supra).

Applicants claims differ in that they require electroencephalogran to identifying the subject in need of such treatment.

However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the Chersey's teaching so as to include a further teaching such as electroencephalogram for identifying the subject with seizure activity as taught in Lerman et al(US 6441156).

US'156(Lerman et al) teaches a calcium channel compositions and its therapeutic uses for the various diseases including epilepsy, see abstract and column 1. Especially US'156 teaches the use of electroencephalogram for assessing the calcium channel defects associated with epileptic episode in human subject , see column 1 and attached sheet(for summary).

Thus, one would have been motivated to use electroencephalogram to identify the human subject who need such treatment because the efficacy and effectiveness of the assay is conventionally known where one could obtain most accurate result with

easy access when the calcium channel blocker are used for the said treatment(i.e. epilepsy). The minor variations including the selection of optimal dosages, routes of administration, or variable applications in order to determine the most effective treatment is well within the skilled level of artisan having ordinary skill in the art, and is obvious. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same (or similar) ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Vickie Kim,
Patent examiner

September 8, 2003
Art unit 1614